

Appendix B

SCIENTIFIC ABSTRACT

Replication incompetent, recombination incompetent retroviral vectors will be used to introduce chemotherapy resistance cDNAs into the normal stem cells of autologous peripheral blood and marrow cells removed and stored following chemotherapy delivered to patients with ovarian cancer who are poor risk (second look positive), and therefore at very high risk of relapse (80%). We estimate that between 0.6 and 2×10^6 CD34 positive cells/kg will be infused and that among these, 10% of the 30% of the total cells infused will be exposed to a MDR-1 containing vector and therefore will be modified with the MDR-1 cDNA. Therefore, 2,000 and 200,000 cells will be marked with MDR-1 cDNA in the autologous cells used for transplant. We will look for the number of MDR-1 marked cells using a methylcellulose late progenitor colony culture system and a PCR assay for the MDR-1 gene used previously. In addition, we will monitor the acquisition of chemotherapy resistance by stem cells of varying degrees of immaturity by using culture assays for these cells under chemotherapy selection (methylcellulose assay and colonies grown from Dexter cultures for more than 35 days, using PCR, antibodies for gp170, and functional assays for the efflux pump coded for by MDR-1). These studies will help us evaluate if introduction of MDR-1 cDNA into peripheral blood or marrow cells will confer chemotherapy resistance on these cells, thus allowing therapy of a greater level of intensity to be delivered and therefore change the course of poor prognosis ovarian cancer.